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Association of Helicobacter Pylori and Liver Hydatid Cyst: A Clinical Case-Control Study

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Original Article

Summary

Hydatid disease is an endemic in Iraq caused by Echinococcal species, Helicobacter pylori is a gram-negative the most common infectious bacterium is strongly linked to the development of duodenal and gastric ulcers , stomach cancer and other alimentary and extra-alimentary diseases. We aimed in this study to assess the association between Helicobacter pylori and liver Hydatid disease. Therefore, a prospective clinical case-control study was conducted including 75 patients with hydatid disease of liver and same number of their close relatives, during the period from first January 2017 to the end of November 2019 at our hospital, both cases and controls were fully investigated and compared. Our findings showed that H. pylori detected in 68% of cases and 22.7% of controls (P<0.001). Females were dominant among patients with positive H. pylori test with female to male ratio of 2.2:1,. Second and third decades of life are more involved in both liver hydatid disease and H. pylori infection. Hydatid patients are most commonly from rural area regardless their affection by H. pylori.

Multiple hydatid cysts are significantly more associated with H. pylori negative test (P. 0.027); also the complication rate of hydatid cysts is mostly occur with those of negative test (P. 0.007). More than three forth of patients with positive H. pylori test were asymptomatic. In conclusion, there is a strong association between liver Hydatid disease and infection with H. pylori.

Keywords: *Liver Hydatid Cyst, Helicobacter Pylori , Epidemiology, Related diseases*

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1. INTRODUCTION

Hydatid disease is a parasitic disease that affects both humans and other mammals, such as sheep, dogs, rodents and horses. There are three different forms of echinococcosis found in humans, each of which is caused by the larval stages of different species of the tapeworm of genus Echinococcus (1).

The first of the three and also the most common form found in humans is cystic echinococcosis (also known as unilocular echinococcosis), which is caused by Echinococcus granulosus. The second is alveolar echinococcosis (also known as alveolar hydatid disease, multilocular echinococcosis), which is caused by Echinococcus multilocularis, and the third is polycystic echinococcosis (also known as human polycystic hydatid disease) which is caused by Echinococcus vogeli and very rarely, Echinococcus oligarthus. Alveolar and polycystic echinococcosis are rarely diagnosed in humans (1). E. granulosus is present virtually worldwide since there are very few countries that are considered to be completely free of E. granulosus. An important fact to keep in mind is that the areas of the world where there is a high incidence of infection by E. granulosus often coincide with rural, grazing areas where dogs are able to ingest organs from infected animals. E. multilocularis mainly occurs in the Northern hemisphere, including central Europe and the northern parts of Europe, Asia, and North America. While alveolar echinococcosis is not extremely common, it is believed that in the coming years, it will be an emerging or re-emerging disease in certain countries as a result of E. multilocularis' ability to spread. Unlike the previous two species of Echinococcus, E. vogeli and E. oligarthus are limited to Central and South America. Furthermore, infections by E. vogeli and E. oligarthus (polycystic echinococcosis) are considered to be the rarest form of echinococcosis (2).

All disease-causing species of Echinococcus are transmitted to intermediate hosts via the ingestion of eggs and are transmitted to definitive hosts by means of eating infected, cyst-containing organs. When thinking about transmission, it is important to remember that humans are accidental intermediate hosts that become infected by handling soil, dirt or animal hair that contains eggs (3).

While there are no biological or mechanical vectors for the adult or larval form of any Echinococcus species, coprophagic flies, carrion birds and arthropods can act as mechanical vectors for the eggs (4).

The incubation period for all species of Echinococcus can be months to years or even decades. It largely depends on the location of the cyst in the body and how fast the cyst is growing. Like many other parasite infections, the course of Echinococcus infection is complex. The worm has a life cycle that requires definitive hosts and intermediate hosts (5,6)

Definitive hosts are normally carnivores such as dogs, while intermediate hosts are usually herbivores such as sheep and cattle. Humans act as accidental hosts, because they are usually a 'dead end' for the parasitic infection cycle.In order to formally diagnose a patient with any type of echinococcosis, one must use a combination of tools that involve imaging techniques, histopathology and/or nucleic acid detection and serology. The imaging technique of choice for cystic echinococcosis is ultrasonography since it is not only able to visualize the cysts in the body's organs but it is also inexpensive, non-invasive and gives instant results. In addition to ultrasonography, both MRI and CT scans are often used (4–7).

For simple cases of cystic echinococcosis, the most common form of treatment is surgical removal of the cysts combined with medical therapy using albendazole and/or mebendazole before and after surgery. However, if there are cysts in multiple organs or tissues, or the cysts are in risky locations, surgery becomes impractical. For inoperable cases such as these, chemotherapy and/or PAIR (puncture-aspiration-injection-reaspiration) become alternative options of treatment (3).

Helicobacter Pylori (H. Pylori)

It is a Gram-negative, microaerophilic bacterium that can inhabit various areas of the stomach, particularly the antrum. It causes a chronic low-level inflammation of the stomach lining and is strongly linked to the development of duodenal and gastric ulcers and stomach cancer. Over 80 percent of individuals infected with the bacterium are asymptomatic. H. pylori infection is most likely acquired by ingesting contaminated food and water and through person to person contact. The infection is more common in crowded living conditions with poor sanitation. Infected individuals usually carry the infection indefinitely unless they are treated with medications to eradicate the bacterium. One out of every six patients with H. pylori infection will develop ulcers of the duodenum or stomach (8).

Symptoms associated with H. pylori can be vague or vary over time. They may be nonspecific, or caused by other conditions. Inflammation of, or damage to the stomach lining (gastritis) by H. pylori may cause mild or serious reactions to the stomach's contents—stomach ache or

abdominal pain, acid reflux, regurgitation, vomiting, belching, flatulence, and nausea. If untreated for a long time, H. pylori infections may be related to several serious illnesses: peptic ulcers (duodenal or gastric ulcers), and cancers of the esophagus and stomach (8).

Diagnostic tests for H. pylori include serology, UBT, SAT and biopsy, however, some variation is found in the detection rates and validity of these tests but all can be used as tests for eradication. Eradication therapy of H. pylori is now routinely given to patients with peptic ulceration. Evidence suggests that if a patient has a peptic ulcer and H. pylori is the principal etiological factor (essentially the patient not taking NSAIDs), complete eradication of the organism will cure the disease and reinfection as an adult is uncommon (9,10).

Also clinical trials showing that cure of infection can cure early stage mucosa-associated lymphoid tissue lymphoma; and reduce the chances of developing gastric cancer in high-risk individuals (11–14).

Helicobacter pylori related diseases

Helicobacter pylori have been implicated in the pathogenesis of numbers of digestive tract disorders, such as atrophic gastritis, peptic ulceration, gastric cancer, and mucosa-associated lymphoid tissue lymphoma (11,15–17)

Also carditis with histologic features similar to those of gastritis in the distal stomach can regard a sequel of H. pylori infection (16,18–20).

Evidence showing possible associations between H. pylori infection in the human stomach and chronic liver diseases is emerging. Many serological studies have found that patients with hepatitis have an increased H. pylori infection rate. Moreover, the prevalence of H. pylori in patients with cirrhosis has been reported to be remarkably higher than in non-cirrhotic patients (21,22). There is an etiological link of H. pylori infection to colorectal neoplasia and the need of routine colonoscopy in seropositive patients (23,24). A study in our country (Iraq) found a relation-ship between H. pylori infection and liver hydatid disease (25).

Therefore we tried to assess the association between H. pylori infection and Hydatid liver disease

2. PATIENTS and METHODS

A clinical case control study including 75 patients with hydatid disease of liver and same number of their close relatives lived in same houses, who were residents of Al-Najaf city in Iraq, at Al-Sadder teaching Hospital, for one year, period from first January 2017 to the end of November 2019.

The data were collected from hydatid liver disease patients, diagnosed by abdominal ultrasound, CT-scan or MRI. The patient were entered the hospital for elective and few for emergent operations of liver hydatid disease or its complications.

The close relatives were investigated by abdominal ultrasound and chest x-ray, to exclude chest or abdominal hydatid disease.

We classified patients with hydatid liver disease into group A1, H. pylori positive test, and group A2, H. pylori negative patients. Their relatives also classified to group B1, positive H. pylori test, and group B2, negative H. pylori test.

All groups are further subdivided according to their age, gender, residence, history of peptic ulcer and history of treatment with antibiotics preoperatively. Data regarding types of liver hydatid cysts (unilocular or multilocular), their locations (right or left lobe), multiplicity and presence or absence of complications including (ruptured, biliary communication and infection) were regarded and analyzed.

H. pylori test was done using Hexagon H. Pylori which has been developed for the rapid diagnosis of H. pylori infections utilizing the detection of antibodies against H. pylori in human serum, plasma and whole blood, independent from antibody classes (IgA, IgG, IgM), within short time.

3. RESULTS

The study showed that among Hydatid cyst patients (n=75), H. pylori test was positive in 51 patients (68%) while in relatives group it was positive in 17 (22.7%) relative persons with highly significant difference, (P. value < 0.001). reflected a strong association between liver Hydatid disease and infection with H. pylori, with an odds ratio (OR of 7.25 indicated that patients with Hydatid cyst were about 7-fold more likely to have H. pylori positive test (Table 1 and Figure 1).

In Hydatid cyst patients, the third and fourth decades were the most common presented age

group, giving 58.8% of cases in H. pylori positive patients, while it composed 50% of patients belong to H. pylori negative tested patients. Females were dominant in H. pylori positive patients compared to H. pylori negative group patients. Hydatid cyst patients were most commonly from rural area regardless their affection by H. pylori, 34 (66.7%) of H. pylori positive and 14 (58.3%) of H. pylori negative patients. Right lobe of liver was the mostly affected site of hydatid cysts (49 patients), while the left lobe is involved in only 7 patients and both lobes are affected in 19 patients. Both lobes are involved more in H. pylori negative patients, 10 patients (41.7%), while they are involved only in 9 (17.6%) of H. pylori positive patients. However, the differences in the demographic characteristics between Hydatid cysts subgroups were statistically insignificant, (P>0.05).

A significant difference was found between H. pylori positive and negative patients regarding their affection number of Hydatid cysts in liver; multiple Hydatid cysts was reported in 18 (35.3%) of the H. pylori positive patients and 62.5% of H. pylori negative patients. Complication rate (ruptured, infected and / or biliary communicated) was more frequent in H. pylori negative, giving significant difference, (p. 0.007). Although, the study shows no significant difference between the two groups regarding their complaints of dyspepsia or history of treatment for already diagnosed peptic ulcer disease, but still more than three forth of patients with positive H. pylori test were asymptomatic. There was no significant difference between patients who received preoperative antibiotics or not, regarding positivity of HEXAGON test, as shown in this study, (P. value > 0.05), (Table 2). In relatives (B1) group, H. pylori test was positive in 10 (19.6%), with no significant differences in age (P>0.05), (Table 3). In relatives (B2) group, H. pylori test was positive in 7 (29.2%), with no significant differences in age (P>0.05), (Table 4).

Table 1. Comparison between groups A and B, regarding H. pylori infection

H. pylori test	Hydatid cyst patients (group A)		Relatives (group B)	
Positive	51	68.0%	17	22.7%
Negative	24	32.0%	58	77.3%
Total	75	100.0%	75	100.0%
P. value < 0.001 Odds ratio (95% CI) = 7.25 (3.51 – 15.0)				

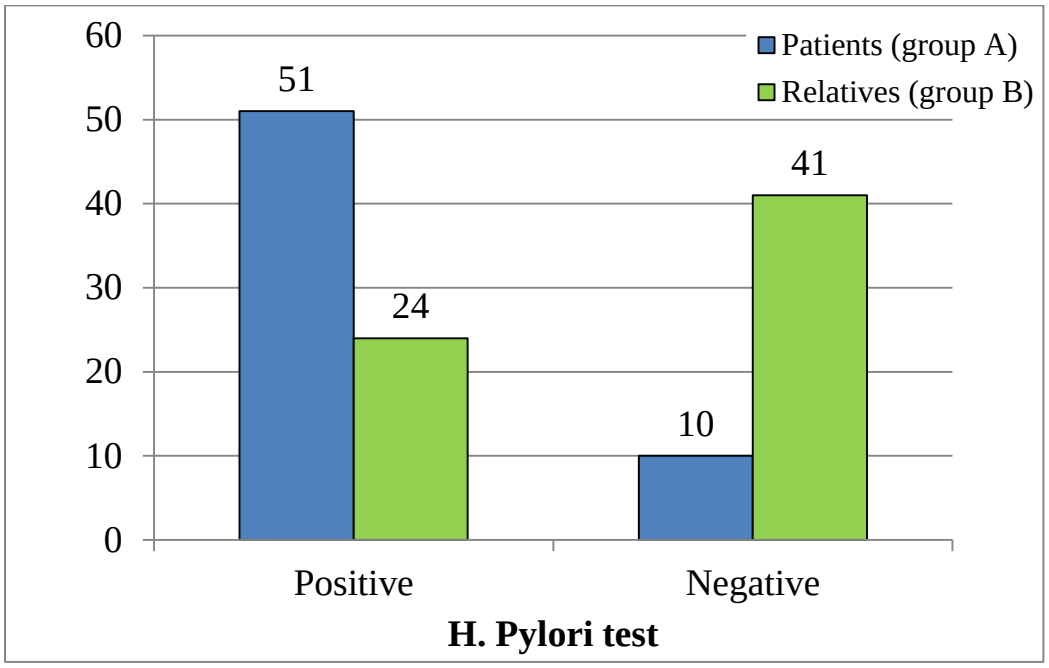

Figure 1. Distribution of H. pylori test results among Hydatid cyst patients and relative groups

Table 2. Characteristics of Hydatid cyst patients (group A1 and A2) according to H. pylori test

Variable		H. pylori positive (n=51)		H. pylori negative (n=24)		P. value
		No.	%	No.	%	
Age	<20	5	9.8	9	37.5	0.059
	20-40	30	58.8	12	50.0	
	> 40	16	31.4	3	12.5	
Gender	Male	16	31.4	13	54.2	0.101
	Female	35	68.6	11	45.8	
Residence	Rural	34	66.7	14	58.3	0.675
	Urban	17	33.3	10	41.7	
Lobe of liver involved	Right	36	70.6	13	54.2	0.067
	Left	6	11.8	1	4.2	
	Both	9	17.6	10	41.7	
Single or multiple Hydatid cysts	Single	33	64.7	9	37.5	0.027
	Multiple	18	35.3	15	62.5	
Complication of Hydatid cyst	Yes	10	19.6	12	50.0	0.007
	No	41	80.4	12	50.0	
History of peptic ulcer or dyspepsia	Yes	12	23.5	3	12.5	0.265
	No	39	76.5	21	87.5	
Pre-operative treatment with antibiotics	Yes	12	23.5	7	29.2	0.600
	No	39	76.5	17	70.8	

Table 3. Age distribution and H. pylori tests of group B1 (relatives of positive H. pylori test patients)

Age (Year)	H. pylori positive test		H. pylori negative test		**Total**
<20	1	20.0	4	80.0	**5**
20-40	9	30.0	21	70.0	**30**
> 40	0	0.0	16	100.0	**16**
Total	10	19.6	41	80.4	**51**

P. value = 0.057

Table 4. Age distribution and H. pylori tests of group B2 (relatives of negative H. pylori test patients)

Age (Year)	H. pylori Positive test		H. pylori Negative test		Total
<20	2	22.2%	7	77.8%	9
20-40	4	33.3%	8	66.7%	12
> 40	1	33.3%	2	66.7%	3
Total	7	29.2%	17	70.8%	24

P. value = 0.847

4. DISCUSSION

Helicobacter pylori (H. pylori) infection has been regarded as the most common infectious disease worldwide. Overall, nearly 50% of the world's population is infected. Surprisingly, most people infected with H. pylori are asymptomatic, The same finding (> 76%) of our patients with Helicobacter pylori positive test were asymptomatic. which suggests that additional factors are necessary for the development of H. pylori–associated diseases (26). Disease outcome is dependent on many factors, including bacterial genotype, host physiology and genetics, and environmental factors such as diet. Researchers continue to explore the complexities of H. pylori infection, seeking to explain why some individuals have asymptomatic infection, whereas others experience clinical disease (26).

Helicobacter pylori have been implicated in the pathogenesis of a number of digestive tract disorders, such as chronic active gastritis, peptic ulceration, gastric cancer, and mucosa-associated lymphoid tissue lymphoma (27).

The importance of treating H. pylori infection in patients with gastrointestinal problems has been confirmed in recent years, with clinical trials showing that cure of infection can prevent duodenal ulcer and, to a lesser extent, gastric ulcer recurrence; cure early stage mucosa-associated lymphoid tissue lymphoma; and reduce the chances of developing gastric cancer in high-risk individuals (27).

Also some extra-digestive system diseases may be associated with it, as it has been mentioned in the introduction, Evidence showing a possible association between H. pylori infection in the human stomach and chronic liver diseases is emerging. Many serological studies have found that patients with hepatitis have an increased H. pylori infection rate. Moreover, the prevalence of H. pylori in patients with cirrhosis has been reported to be remarkably higher than in non-cirrhotic patients (28).

Also a few papers have recently reported that H. pylori caused liver damages as an independent etiological factor, and that the gene belonging to it was demonstrated by PCR in mice (28).

This will highlight our thinking about the possibility of association between liver hydatid disease and infection with H. pylori, and to answer the question regarding the combined effect on stomach and upper small bowel (by inflammation and weakening of their mucosa) and that effect on liver, both, may facilitate the entrance of the Echinococcus parasite throw

the diseased bowel mucosa and infecting the diseased liver, causing liver hydatid disease.

We found only one published research to identify the relationship between H. pylori and Hydatid disease in world which is done on IRAQ / Al-Najaf city (25), which give us an appreciation to progress in our research. In this study Fifty eight patient with hydatid liver disease 30 male (51.7%) and 28 female (48.3%) were screened for presence of H. pylori infection by using ELISA test, found 28 patient have positive ELISA test of them 19 male (32.75%) and 9 female (15.51%), finally this research confirm that (48.27) % of all hydatid infected patient have H. pylori infection. Also this study showed that patients with single cyst and positive with H. pylori are 18 of 28 (64.29%), while the patients with more than one cyst (multiple) and positive for ELISA test are 10 of 28 (35.71%) (25).

Out of 75 patients and their relatives (75 liver hydatid diseased patients and 75 of their relatives) was taken in our study, 68% of the hydatid diseased patients have positive H. pylori detection test, while their relatives have positive test of Helicobacter pylori in 22.7%, using (HEXAGON H. PYLORI rapid test), which showed, when compared to an anti-H. Pylori IgG ELISA, an average diagnostic sensitivity of 97% and an average diagnostic specificity of 93% (29).

So there was great relationship between hydatid liver disease and the infection by H. pylori (p. value <0.001). Although not so significant, in hydatid liver cysts infected patients who have had positive H. pylori test, females were more than males (69%: 31%), while in A2 group showed no significant differs regarding gender, so females with H. pylori infections were more susceptible for hydatid liver disease. It is especially in poor or rural families, where the Hydatid and H. pylori infection more common, the female housewives are more liable for the transmitting and acquiring the micro-organism due to their house works. Regarding multiplicity of Hydatid liver cysts, single cyst was more in group A1 and multiple cysts significantly more than single cysts in group A2, p. value is 0.027. This result is nearly similar to the finding which was discussed in above mentioned study, patients with single cyst and positive with H. pylori are 18 of 28 (64.29%), while the patients with more than one cyst (multiple) and positive for ELISA test are 10 of 28 (35.71%) (25).

Also in group A1 the cases of complicated hydatid cysts are less than non complicated cases, while in group A2 the complicated and non-complicated are equal. The complicated cases were strongly associated with negative test result (p. 0.007).

The association of multiplicity and complication of Hydatid disease with negative result of H. pylori infection could be due to aggressive behavior of the parasite or less effective immune defense of infected patients, that the parasite can enter upper gastrointestinal mucosa without need for help of H. pylori, really, needs further researches for explanation.

5. CONCLUSIONS

1. There is a significant positive relationship between the infection with H. pylori and the liver Hydatid disease.
2. The second and third decades are the more presenting age in both hydatid liver disease and H. pylori infection.
3. Peoples who are lived in rural area are more liable to, both, infection with H. pylori and liver Hydatid cysts.
4. The female gender has positive effect on the relation between H. pylori and liver Hydatid disease, while Hydatid cyst complication and multiplicity can negatively affect this relationship.
5. Most H. pylori infected cases are a symptomatic

Ethical Clearance: Ethical clearance and approval of the study are ascertained by the authors. All ethical issues and data collection were in accordance with the World Medical Association Declaration of Helsinki 2013 of ethical principles for medical research involving human subjects. Data and privacy of patients were kept confidentially.

Conflict of interest: Authors declared none

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